

**ABSTRACT**

The present invention is directed to novel soluble substrates for  $\gamma$ -secretase. More particularly, the invention provides a soluble fusion polypeptide with a Notch segment containing  
5 the  $\gamma$ -secretase-dependent cleavage sites ( $\gamma$  and  $\epsilon$ ) fused to a NusA protein. Methods and compositions for making and using such a fusion protein are disclosed.